

**TRANSLATION**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

|   |   |   |
|---|---|---|
| Applicant's or agent's file reference<br><b>PCT-0414</b>  | <b>FOR FURTHER ACTION</b>                                       | See Form PCT/IPEA/416                               |
| International application No.<br><b>PCT/JP2004/013768</b>   | International filing date (day/month/year)<br><b>21.09.2004</b> | Priority date (day/month/year)<br><b>22.09.2003</b> |
| International Patent Classification (IPC) or national classification and IPC<br><b>C07D211/58, 401/06, 401/14, 401/02, 401/12, 409/12, A61K31/4545, 31/496, 31/454, 31/4523</b> |   |   |
| Applicant<br><b>BANYU PHARMACEUTICAL CO., LTD.</b>  |   |   |

|   |                                   |   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
|---|-----------------------------------|---|-----------|---------------------|--------------------------|------------|----------|--------------------------|-------------|--|--------------------------|------------|----------------------------|-------------------------------------|-----------|---|-------------------------------------|------------|-------------------------|--------------------------|-------------|--|--------------------------|--------------|---|
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> |                                   |   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <p>4. This report contains indications relating to the following items:</p> <table><tr><td><input checked="" type="checkbox"/></td><td>Box No. I</td><td>Basis of the report</td></tr><tr><td><input type="checkbox"/></td><td>Box No. II</td><td>Priority</td></tr><tr><td><input type="checkbox"/></td><td>Box No. III</td><td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td></tr><tr><td><input type="checkbox"/></td><td>Box No. IV</td><td>Lack of unity of invention</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. V</td><td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td></tr><tr><td><input checked="" type="checkbox"/></td><td>Box No. VI</td><td>Certain documents cited</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VII</td><td>Certain defects in the international application</td></tr><tr><td><input type="checkbox"/></td><td>Box No. VIII</td><td>Certain observations on the international application</td></tr></table>  |                                   | <input checked="" type="checkbox"/>   | Box No. I | Basis of the report | <input type="checkbox"/> | Box No. II | Priority | <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/>   | Box No. I                         | Basis of the report   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input type="checkbox"/>  | Box No. II                        | Priority  |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input type="checkbox"/>  | Box No. III                       | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input type="checkbox"/>  | Box No. IV                        | Lack of unity of invention  |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input checked="" type="checkbox"/>   | Box No. V                         | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input checked="" type="checkbox"/>   | Box No. VI                        | Certain documents cited   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input type="checkbox"/>  | Box No. VII                       | Certain defects in the international application  |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| <input type="checkbox"/>  | Box No. VIII                      | Certain observations on the international application   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| Date of submission of the demand  | Date of completion of this report |   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| Name and mailing address of the IPEA/JP   | Authorized officer                |   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |
| Facsimile No.   | Telephone No.                     |   |           |                     |                          |            |          |                          |             |  |                          |            |                            |                                     |           |   |                                     |            |                         |                          |             |  |                          |              |   |

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/013768

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_ as originally filed/furnished
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- nos. \_\_\_\_\_ as originally filed/furnished
- nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- sheets \_\_\_\_\_ as originally filed/furnished
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

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| Box No. V   | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |              |     |
|---|---|--------------|-----|
| 1. Statement  |   |              |     |
| Novelty (N)   | Claims  | 3-15         | YES |
|   | Claims  | 1, 2         | NO  |
| Inventive step (IS)   | Claims  | 3-10, 13-15  | YES |
|   | Claims  | 1, 2, 11, 12 | NO  |
| Industrial applicability (IA)   | Claims  | 1-15         | YES |
|   | Claims  |              | NO  |
| 2. Citations and explanations (Rule 70.7)   |   |              |     |
| Document 1: WO 02/099388 A2   |   |              |     |
| Document 2: JP 10-324695 A  |   |              |     |
| Document 3: JP 5-78316 A  |   |              |     |
| Document 4: WO 02/076925 A2   |   |              |     |
| Document 5: JP 2001-522836 A  |   |              |     |
| I. Claims 1 and 2   |   |              |     |
| <p>The invention set forth in claims 1 and 2 lacks novelty and does not involve an inventive step in the light of document 1 or document 2.</p>   |   |              |     |
| <p>The compounds disclosed in document 1 (examples 2 and 3) and the compounds disclosed in document 2 (preparation example 219) include the compounds that are represented by general formula (I) set forth in the present application.</p> |   |              |     |
| II. Claims 11 and 12  |   |              |     |
| <p>The inventions set forth in claims 11 and 12 do not involve an inventive step in the light of document 1.</p>  |   |              |     |
| <p>Document 1 indicates that the compounds represented by formula (I) are effective against diseases such as diabetes, hyperlipemia and Alzheimer's disease (refer to page 21, line 1 to page 24, line 21), and thus it would</p>           |   |              |     |

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

have been easy for a person skilled in the art to conceive of attempting to confirm whether the compounds set forth in examples 2 and 3, which are specific examples of compounds that are represented by formula (I), exhibit a pharmacological activity in relation to the abovementioned diseases.

## III. Claims 3 to 10 and 13 to 15

The inventions set forth in claims 3 to 10 and 13 to 15 are novel and involve an inventive step in relation to documents 1 to 5.

The compounds set forth in claims 3 to 10 of the present application are not disclosed or suggested in either document 1 or document 2.

Meanwhile, document 3 discloses 4-piperidinyl piperidine derivatives wherein a phenyl group has been bonded to the nitrogen atom; however, document 3 does not disclose or suggest the compounds that are set forth in claims 3 to 10 of the present application.

In addition, documents 4 and 5 disclose compounds that exhibit an antagonizing action in relation to the histamine H3 receptor; however, the base structures thereof differ from the base structures of the compounds that are set forth in the present application.

Furthermore, it cannot be considered to have been easy for a person skilled in the art to conceive of the compounds that are set forth in claims 3 to 10 of the present application, even with consideration of the disclosures in documents 1 to 5.

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## Box No. VI Certain documents cited

## 1. Certain published documents (Rule 70.10)

| Application No.<br>Patent No. | Publication date<br>(day/month/year) | Filing date<br>(day/month/year) | Priority date (valid claim)<br>(day/month/year) |
|-------------------------------|--------------------------------------|---------------------------------|---|
| WO 04/037257 A1<br>[EX]       | 06.05.2004                           | 23.10.2003                      | 23.10.2002                                      |
| WO 04/069792 A2<br>[EX]       | 19.08.2004                           | 02.02.2004                      | 03.02.2003                                      |

## 2. Non-written disclosures (Rule 70.9)

| Kind of non-written disclosure | Date of non-written disclosure<br>(day/month/year) | Date of written disclosure<br>referring to non-written disclosure<br>(day/month/year) |
|--------------------------------|--|---|
|--------------------------------|--|---|

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International application No.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

The Cover Sheet

International Patent Classification (IPC) or national  
classification and IPC:

(IntCl<sup>7</sup>) 31/4535, 31/506, A61P43/00, 3/04, 3/10, 5/00,  
3/06, 19/06, 9/10, 9/04, 9/12, 13/12, 25/20, A61P25/24,  
25/22, 25/08, 25/18, 25/28, 25/16, 25/02, 25/32, 25/36